Osteoporosis Int (1996) 6:8–13


**Osteoporosis International**

*Original Article*

# Computed Radiographic Absorptiometry and Morphometry in the Assessment of Postmenopausal Bone Loss

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**Abstract.** The best method for the diagnosis of osteoporosis and assessment of fracture risk is currently considered to be bone densitometry. The most commonly used dual-energy X-ray absorptiometry (DXA) methods may sometimes not predict bone mass accurately in every skeletal site, are expensive and not widely available. The recent development of computed analysis of a plain radiograph of the hand might provide a practical, inexpensive and rapid method for evaluation of bone mineral status. In this study we evaluated 20 healthy premenopausal and 660 postmenopausal women. In 36 of these subjects a second evaluation was carried out after 2 years of therapy with calcium supplements. The internal and external diameters of the second metacarpal and the metacarpal and ultradistal radial bone density were evaluated using a technical device developed in our laboratory and marketed by NIM, Verona, Italy (Osteoradiometer). The radiographic images, captured by a video camera, were digitized and studied by computed analysis. In 150 subjects bone density at the level of the lumbar spine, femur, and ultradistal and proximal radius was also measured by DXA techniques. Both external ($D$) and internal ($d$) diameters increase significantly with age and years since menopause (YSM), whereas metacarpal index ($D - d/D$) and metacarpal and ultradistal radial bone density decrease significantly with age and YSM. The ratio between metacarpal bone mineral content and the cortical area (volumetric metacarpal bone density) did not change with age. Significant correlations were found between radiometric findings and DXA measurements. The best correlation coefficients were between bone density measured at the level of the ultradistal radius by DXA and radiographic absorptiometry. In the 2-year follow-up study, a 4.9% and 6.2% decline in radial metacarpal bone density respectively were observed, but the difference was statistically significant only for the latter. In conclusion, computed radiogrammetry is closely correlated with all DXA measurements and may be useful in screening of large populations, providing a simple, inexpensive and sufficiently precise method for evaluation of bone mineral status. Further studies are warranted for assessing the accuracy of radiogrammetry for longitudinal investigations and its capacity to predict fracture risk.

**Keywords:** Dual-energy X-ray absorptiometry; Osteoporosis; Radiogrammetry; Radiographic absorptiometry

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## Introduction

Osteoporosis is a disorder characterized by decreased bone mass and consequent increased susceptibility to fracture [1]. Bone densitometry is currently considered the best method for diagnosis of osteoporosis and assessment of fracture risk [2–4]. The most commonly used methods include single-photon absorptiometry (SPA), dual-photon absorptiometry (DPA), quantitative computed tomography (QCT) and dual-energy X-ray absorptiometry (DXA). SPA measures peripheral bone mass (the forearm) and may not accurately predict bone mass in the axial skeleton [5]. DPA, DXA and QCT measure bone mass of the axial and peripheral skeleton, but the measurements are time-consuming, expensive, and require a large amount of space for the machinery. QCT in addition entails much greater

radiation exposure of the subject than the other techniques [6].

A reasonable, accurate, less costly and more widely accessible method for assessing bone mineral status would be useful for screening large populations in order to identify those subjects for whom therapeutic intervention is required.

The evaluation of cortical thickness and of bone density from a radiograph of the hand preceded all the above techniques as a way of estimating bone density and bone loss [7,8], but this technique has been neglected due to its poor accuracy and reliability [9] in unskilled hands or when the measurements are carried out by different operators [10]. The more recent availability of computed analysis of digitized images has improved the precision and accuracy of the measurements and this may provide a practical, inexpensive and rapid way of determining bone mineral mass.

In this study we evaluated both cortical thickness and bone density from radiographs of the hand using computerized X-ray analysis system developed in our laboratory. The data were compared with those obtained by assessing bone density with standard techniques.

## Subjects and Methods

### *Subjects*

The study group consisted of 20 healthy premenopausal volunteers (nurses and doctors of our department), aged 35–42 years, and 660 postmenopausal women aged 40–86 years (59 ± 8 years) not receiving drugs which are known to affect bone status and/or calcium metabolism. The postmenopausal women were, on average, 11 ± 8 (range 1–39) years since menopause (YSM).

The postmenopausal subjects were randomly recruited from the community to participate in a health survey of postmenopausal women organized by our health authority and focused mainly on osteoporosis risk assessment. They were generally in good health and able to attend our clinic.

In 36 of these subjects (aged 58–72 years) a second evaluation was carried out after 2 years of therapy with 500 mg/day calcium supplement (Calcium Sandoz Forte, Sandoz, Italy) prescribed because of mild osteopenia (spine bone density range 700–790 mg/cm$^2$).

### *Methods*

Standard antero-posterior X-ray images of the non-dominant hand and distal forearm were taken with fine-grain films (usually used for mammography). Radiographs were taken at a standard kilovoltage setting (45 kvp for 1 s, at 300 mA) using non-screened 3M film. Focus–film distance was maintained within a narrow range (120–130 cm). A graduated aluminium reference standard calibrated against a hydroxyapatite phantom was positioned at the level of the styloid process (Fig. 1) so that bone and phantom were symmetrical around the central axis of the X-ray beam. The X-ray pictures were analyzed using a technical device (Osteoradiometer, NIM, Verona, Italy) developed in our laboratory.

With this technique, the radiographic images are "captured" by a video camera and the grey levels of the digitalized image can be quantified against the reference standard (radiographic absorptiometry, RA). Digital image resolution is 512 × 512, with 256 grey levels. A conversion factor of 0.3 mm/pixel is obtained. The definition of the cortical bone edges is based on analysis of the grey levels at the line crossing perpendicularly exactly at the midpart of the metacarpal bones. From the algorithm describing the changes in grey levels, an arbitrary threshold slope was adopted in order to identify consistently the outer and inner diameter of the long bones. The aluminium phantom was positioned close to the two sites where bone density had to be measured. The image acquisition and evaluation of all indices listed below could be performed within 3 min by even a relatively unskilled operator. The operator simply defines on the screen the proximal and distal ends of the metacarpus and the distal end of the radius and a computer program then computes all the indices automatically.

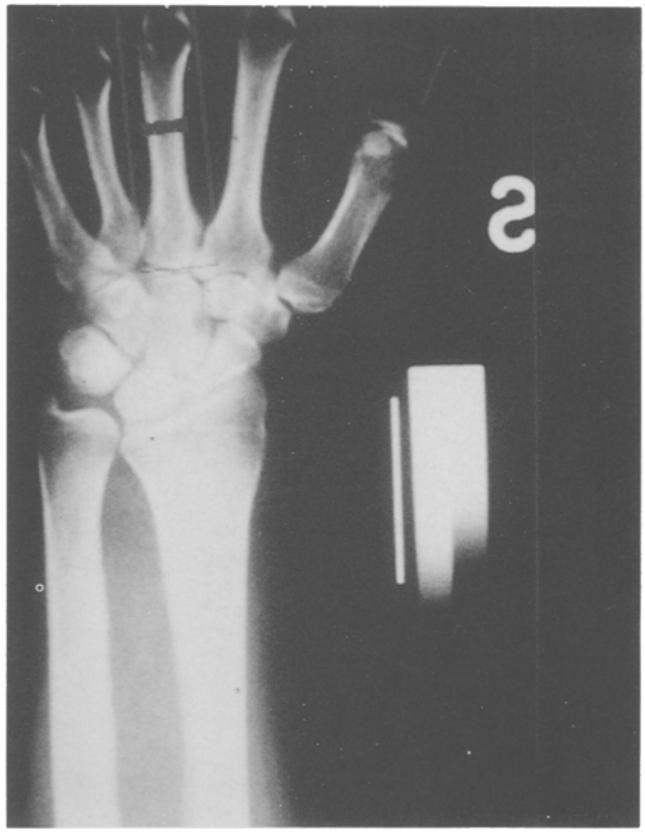

**Fig. 1.** X-ray image of the left hand with an aluminium phantom for length and density evaluation. The region of interest for metacarpal density is also shown.

The outer diameter ($D$) and inner diameter ($d$) of all metacarpals, the bone density of their middle region ($RA_{met}$, mg/cm$^2$) and bone density of the ultradistal radius ($RA_{rad}$, mg/cm$^2$) were measured. In addition, assuming a circular cross-sectional area for the metacarpals, the following parameters could be computed:

Metacarpal index (MI) = $(D - d)/D$

Medullary area (MA) = $(d/2) \times (d/2) \times 3.14$

Metacarpal cortical area (MCA) = $(D/2) \times (D/2) \times 3.14 - MA$

Bone mineral content corrected for the cross-sectional area (volumetric bone density, $vRA_{met}$, mg/cm$^3$) of metacarpals = $BMC_{met}/MCA$

The coefficient of variation (CV%) for radiometric measurements was evaluated in 58 subjects (aged 53–75 years) in whom standard radiographs of the hand were taken in two different laboratories, 1–4 months apart.

Forearm bone density was measured at proximal ($DXA_{pr}$) and ultradistal ($DXA_{ud}$) sites by DXA (Osteoscan-NIM, Verona, Italy). The reproducibility of the DXA equipment was determined by repeated measures, 0.5–2 months apart, on 12 subjects, and the resulting CVs were 0.77% for the ultradistal and 0.67% for the proximal site.

Spinal bone density, at the level of the lumbar spine (L2–4) in the antero-posterior projection ($DXA_{spine}$), and femoral bone density at the level of the neck ($DXA_{neck}$), Ward's triangle ($DXA_{ward}$) and trochanter ($DXA_{troc}$), were measured by DXA (L–XRA Sophos, France). The CV was <1.5% at all above sites in a non-routine setting.

Simple and multiple regression, and the significance of differences, were assessed by a computer program (Statgraph, USA). For all statistical tests significance was defined as $p<0.05$.

## Results

The CVs and the correlation matrix with age or DXA measurements of bone mass indices measured at the first, third and fifth metacarpals were very poor. The CVs of the fourth metacarpals indices was only marginally inferior to that of the second metacarpals. By averaging the indices obtained at the second and fourth metacarpals the overall CV did not improve and the correlations with DXA measurements worsened. For these reasons we report here only the data obtained at the level of the second metacarpal.

CV% was 1.5%, 1.1% and 1.8% for the MI, $RA_{met}$ and $RA_{rad}$ respectively when the measurements were performed by two different operators on the same 58 radiographs. The inter-radiograph CV% was 5.0%, 5.1% and 6.9% for MI, $vRA_{met}$ and $RA_{rad}$ respectively (Table 1). The CV has been divided by the range over mean ratio to give a measure that quantifies the potential of each measurement parameter to discriminate between individuals of different status. This new index [11] will be referred to as the standardized coefficient of variation (SCV) (Table 1).

MI declined significantly with age. This appears to be due to a progressive increase in the inner diameter, despite a continuous significant enlargement with age of the external diameter (Table 2).

The density measurements obtained from the computed evaluation of the hand radiographs from the 660 postmenopausal women were significantly correlated with both age and YSM (Table 2, Fig. 2). For all parameters the extrapolated value to YSM = 0 was very close to the mean values found in premenopausal women (Table 3).

Significant correlations were found between the radiometric findings (radiographic absorptiometry, RA and MI) and the DXA measurements performed in 150 subjects; the correlation coefficients remained statistically significant even after exclusion of the effect of age by partial correlation (Table 4). The best correlation ($r = 0.77$) was found between $RA_{rad}$ and $DXA_{ud}$, reflecting the fact that the measurements were performed at the same skeletal site. The second-best

**Table 2.** Correlation coefficients ($r$) between age or logarithm of years since menopause (ysm) and bone findings measured by quantitative radiogrammetry at the second metacarpal and ultradistal radius of the non-dominant hand

| | $D$ | $d$ | MI | $RA_{met}$ | $vRA_{met}$ | $RA_{rad}$ |
|---|---|---|---|---|---|---|
| Age | 0.15 | 0.46 | −0.46 | −0.39 | NS | −0.31 |
| Age | 0.1 | 0.32 | −0.35 | −0.35 | NS | −0.36 |

$D$, outer diameter of the second metacarpal; $d$, medullary diameter of the second metacarpal; MI, metacarpal index; $RA_{met}$, bone density of mid metacarpal, mg/cm$^2$; $vRA_{met}$, metacarpal bone mineral content/metacarpal cortical area, mg/cm$^3$; $RA_{rad}$, bone density of ultradistal radius, mg/cm$^2$

**Table 1.** Overall results for each of the three main radiogrammetry parameters

| Radiogrammetry parameter | Mean | Range (5%–95%) | Range/mean (%) | Intra-radiograph CV (%) | Intra-radiograph SCV (%) | Inter-radiograph CV (%) | Inter-radiograph SCV (%) |
|---|---|---|---|---|---|---|---|
| MI | 0.51 | 0.38–0.67 | 57 | 1.5 | 2.6 | 5.0 | 8.8 |
| $RA_{met}$(mg/cm$^2$) | 408 | 295–519 | 54 | 1.0 | 2.0 | 5.1 | 9.3 |
| $RA_{rad}$(mg/cm$^2$) | 331 | 220–423 | 73 | 1.8 | 2.4 | 6.9 | 9.4 |

The data shown are: the mean, the range, shown as the 5th to 95th percentile, the inter- and intra-radiograph coefficient of variation (CV), the ratio of the range over mean, and the standardized coefficient of variation (SCV), which describes the effective precision of the equipment. MI, metacarpal index; $RA_{met}$, bone density of mid metacarpus, mg/cm$^2$; $RA_{rad}$, bone density of ultradistal radius, mg/cm$^2$.

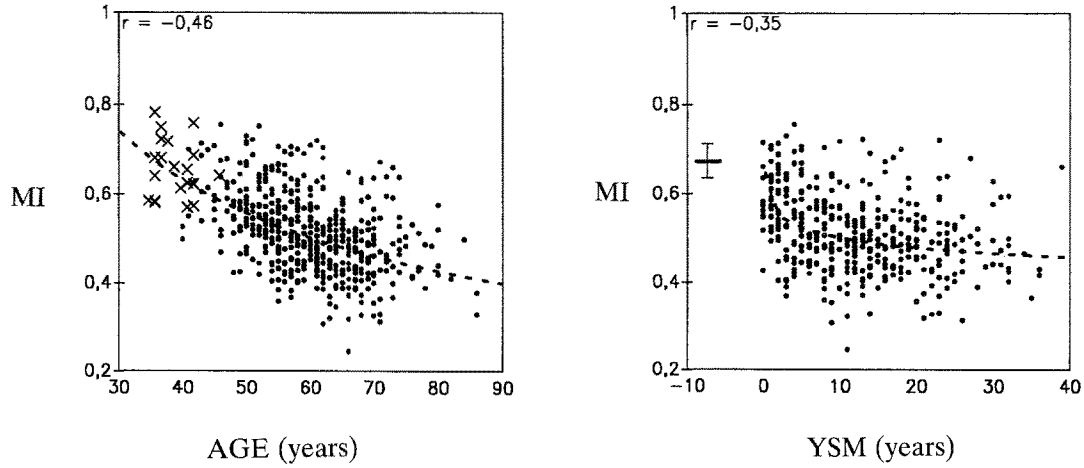


**Fig. 2.** Correlation between metacarpal index (MI) versus age (*left-hand panel crosses*, premenopausal subjects) and years since menopause (YSM, *right-hand panel*). The mean and SD value for premenopausal women are also shown.

**Table 3.** Quantitative radiogrammetry values (mean and SD) in premenopausal women

| | *D* (mm) | *d* (mm) | MI | $RA_{met}$ (mg/cm²) | $vRA_{met}$ (mg/cm³) | $RA_{rad}$ (mg/cm²) |
|---|---|---|---|---|---|---|
| Average | 8.8 | 3.5 | 0.68 | 472 | 87.5 | 400 |
| SD | 0.76 | 0.76 | 0.07 | 59 | 13.4 | 56 |

See Table 1 for abbreviations.

**Table 4.** Correlation matrix (*r* and standard error of estimate, % of premenopausal value) between the quantitative radiogrammetry data and densitometric values as measured by DXA

| | MI | $RA_{met}$ | $vRA_{met}$ | $RA_{rad}$ |
|---|---|---|---|---|
| $DXA_{spine}$ | 0.50 (11.7%) | 0.43 (15.2%) | 0.13 (15.1%) | 0.49 (14.7%) |
| $DXA_{neck}$ | 0.45 (11.7%) | 0.38 (16.2%) | NS | 0.47 (14.8%) |
| $DXA_{ward}$ | 0.45 (11.7%) | 0.44 (15.7%) | 0.20 (15.6%) | 0.52 (14.4%) |
| $DXA_{troc}$ | 0.28 (13.2%) | 0.40 (16.2%) | 0.25 (15.6%) | 0.32 (16.3%) |
| $DXA_{ud}$ | 0.46 (13.2%) | 0.67 (10.9%) | 0.29 (12.8%) | 0.77 (12.1%) |
| $DXA_{pr}$ | 0.51 (13.2%) | 0.76 (9.5%) | 0.39 (12.1%) | 0.65 (14.5%) |
| MI | – | 0.58 (14.7%) | NS | 0.48 (15.0%) |
| $RA_{met}$ | 0.58 (11.7%) | – | 0.74 (10.4%) | 0.52 (14.1%) |

See Table 1 and text for abbreviations.

correlation coefficient ($r = 0.76$) was found when the DXA values were correlated with the densities at in two cortical sites ($RA_{met}$, $DXA_{pr}$) using the Osteoradiometer. The volumetric density at the metacarpals ($vRA_{met}$) was significantly correlated with most of the DXA measurements, but was correlated neither with age nor with YSM.

In the subjects in whom the measurements were repeated 2 years later, a 4.9% and 6.2% decline in radial and metacarpal bone density respectively were observed, but this difference achieved statistical significance (paired *t*-test and test for location) only for the latter. The MI did not change significantly during the 2-year period (Table 5).

**Table 5.** Percentage changes (median and 10th + 90th percentiles) of the metacarpal index (MI) and radiographic absorptiometry of the second metacarpal and distal radius in postmenopausal women treated for 2 years with 500 mg calcium supplements

| | Median | Percentiles | | *p* |
|---|---|---|---|---|
| | | 10th | 90th | |
| MI | 1.5 | −15 | 20 | NS |
| $RA_{met}$ | −6.2 | −21 | 0 | 0.03 |
| $RA_{rad}$ | −4.9 | −15 | 12 | NS |

The significance was assessed by a non-parametric method (test for location based on signs). See Table 1 and text for abbreviations.

## Discussion

Radiographic absorptiometry and radiogrammatory used to be the only techniques for assessing bone status, but they were abandoned when photon and X-ray absorptiometry became available. More recently [12–14], the development of computed analysis of digitized X-ray pictures has focused attention on this easily available and inexpensive technique. With the apparatus developed in our laboratory a reasonably precise evaluation of cortical thickness and bone density in several sites can be obtained.

Cortical thickness may provide an accurate estimation of fracture risk [15,16]. The metacarpal index, described by Barnett and Nordin [17], normalizes the cortical thickness for the metacarpal width and can be used for assessing cortical bone loss. Visual measure-

ment of the internal and external diameters of long bones is tedious, time-consuming, observer-dependent and has poor intra-observer reproducibility, ranging from 3.1% [10,16] to 11% [9], which precludes its use for sequential evaluations. The availability of automated computerized radiogrammetry of the metacarpals decreases the coefficient of variation to less than 2% – a value comparable to that observed with similar techniques by others [18].

In this study we have shown that the MI is closely correlated with all DXA measurements even after correction for age, even though the correlation coefficients we found exclude the possibility of predicting one bone mass index from another on an individual basis. As expected, the best correlation coefficients were detected with the cortical skeletal sites ($DXA_{pr}$ and $RA_{met}$), but MI appears to predict significantly all other DXA mesurements (Table 4). The correlation coefficients we observed are of the same order of magnitude as those found in other studies using a similar computed radiogrammetry technique [18,19].

We have confirmed in this study that the external diameter of the metacarpals increases significantly with age, and this might be responsible for an underestimate of the rate of loss with ageing as measured by densitometric procedures [20].

The bone density measured at metacarpal and radial sites was well correlated with the values found by DXA at the level of the spine, femur and forearm. As expected, $RA_{rad}$ was correlated best with $DXA_{ud}$, but there was no obvious preferential predictivity of $RA_{rad}$ and $RA_{met}$ for the skeletal sites were trabecular or cortical bone respectively were most represented. The correlation matrix (Table 4) for the different bone mass measurement sites we found is similar to those recently reported by Kleerkoper et al. [21] who made use of a radiographic absorptiometry technique limited to the middle phalanx of a finger.

The precise definition of the inner diameters of a long bone that can then be achieved with computed radiogrammetry allows the evaluation of the volumetric metacarpal bone density ($vRA_{met}$). This reflects the real density ($mg/cm^3$) of cortical bone that cannot be assessed by DXA. $vRA_{met}$ was poorly correlated with DXA measurements and not at all with age or YSM (Table 2). This indicates that most of the changes with ageing in the so-called bone density measured by DXA or SPA in cortical bone are due to the diminution of bone volume rather than density. This again emphasizes the importance of the MI in the evaluation of cortical bone trophism.

The intra-radiograph, inter-observer CV for MI was comparable to that found by others [18,19] but the CV for radiographic absorptiometry was somewhat higher (0.63% versus 1.1–1.8%) than that found using the CompuMed technique. With this procedure the examination is limited to the middle phalanx of the index finger, offering the advantage of positioning the aluminium phantom much closer to the region of interest. On the other hand, our technique has the potential to evaluate bone density in several more clinically relevant sites and to measure the MI.

For large-scale diagnostic screening and for follow-up studies, the CV should be assessed between different radiographs, and this has never been thoroughly assessed. With our apparatus, the CV between radiographs taken by two different machines was in the order of 5%–7% for all parameters, and this could not be substantially improved by averaging the values obtained in two metacarpal bones. In any case, these errors appear acceptable for large-scale population screening and may not be of critical relevance (0.4–0.5 SD of the premenopausal levels) for the diagnosis of osteoporosis or for the identification of therapeutic threshold [1]. The standardized inter-radiograph CV (SCV) is higher than that for DXA measurements (~2.2%) but somewhat lower than the SCV found for ultrasonic velocity measurements [11]. The inter-radiograph CV is of the same order of magnitude or even greater than the percentage declines observed within 2 years in a group of postmenopausal women (Table 4). These changes were statistically significant only for $RA_{met}$, but the inability of MI and $RA_{rad}$ to detect significant changes in this study might be due to the relatively small number of observations and/or the low expected rate of bone loss in late postmenopausal women treated with calcium supplements [22,23].

In conclusion, computed radiogrammetry may be of help in large-scale population screening since it allows the acquisition of several indices of skeletal mass from a simple radiograph of the hand. The precision of radiogrammetry for longitudinal studies remains questionable. Further studies are also warranted to assess the accuracy of radiogrammetry in the diagnosis of osteoporosis, which can only be achieved by showing its predictivity for future fractures.

*Acknowledgements.* We are grateful to the medical staff of ULSS 7 (Valle dell'Agno) of the Veneto Region for referring patients and X-ray pictures to our centre for the study.

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*Received for publication 27 December 1994*
*Accepted in revised form 8 June 1995*